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 NEWS  2  Sep 17  IMSworld Pharmaceutical Company Directory name change
                  to PHARMASEARCH
 NEWS  3  Oct 09  Korean abstracts now included in Derwent World Patents
                  Index
 NEWS  4  Oct 09  Number of Derwent World Patents Index updates increased
 NEWS  5  Oct 15  Calculated properties now in the REGISTRY/ZREGISTRY File
 NEWS  6  Oct 22  Over 1 million reactions added to CASREACT
 NEWS  7  Oct 22  DGENE GETSIM has been improved
 NEWS  8  Oct 29  AAASD no longer available
 NEWS  9  Nov 19  New Search Capabilities  USPATFULL and USPAT2
 NEWS 10  Nov 19  TOXCENTER(SM) - new toxicology file now available on STN
 NEWS 11  Nov 29  COPPERLIT now available on STN
 NEWS 12  Nov 29  DWPI revisions to NTIS and US Provisional Numbers
 NEWS 13  Nov 30  Files VETU and VETB to have open access
 NEWS 14  Dec 10  WPINDEX/WPIDS/WPIX New and Revised Manual Codes for 2002
 NEWS 15  Dec 10  DGENE BLAST Homology Search
 NEWS 16  Dec 17  WELDASEARCH now available on STN
 NEWS 17  Dec 17  STANDARDS now available on STN
 NEWS 18  Dec 17  New fields for DPCI
 NEWS 19  Dec 19  CAS Roles modified
 NEWS 20  Dec 19  1907-1946 data and page images added to CA and CAplus
 NEWS 21  Jan 25  BLAST(R) searching in REGISTRY available in STN on the Web
 NEWS 22  Jan 25  Searching with the P indicator for Preparations
 NEWS 23  Jan 29  FSTA has been reloaded and moves to weekly updates
 NEWS 24  Feb 01  DKILIT now produced by FIZ Karlsruhe and has a new update
                  frequency
 NEWS 25  Feb 19  Access via Tymnet and SprintNet Eliminated Effective 3/31/02
 NEWS 26  Mar 08  Gene Names now available in BIOSIS

 NEWS EXPRESS  February 1 CURRENT WINDOWS VERSION IS V6.0d,
               CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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=> s lonberg N?/au or Kay/Au
L1          160 LONBERG N?/AU OR KAY/AU

=> s l1 and CD4
L2           16 L1 AND CD4

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3           11 DUP REM L2 (5 DUPLICATES REMOVED)

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=> dis l3 1-11 ibib abs
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L3 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:152726 CAPLUS
DOCUMENT NUMBER: 134:206569
TITLE: Human CTLA-4 antibodies and their uses
INVENTOR(S): Korman, Alan J.; Halk, Edward L.; **Lonberg, Nils**
PATENT ASSIGNEE(S): Medarex, Inc., USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014424	A2	20010301	WO 2000-US23356	20000824
WO 2001014424	A3	20010920		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-150452 P 19990824

AB The present invention provides novel human sequence antibodies against human CTLA-4 and methods of treating human diseases (e.g. cancer, allergy, inflammation, autoimmune disease, graft vs. host disease, Alzheimer's disease), infections and other conditions using these antibodies.

L3 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:741488 CAPLUS
DOCUMENT NUMBER: 135:302905
TITLE: Transgenic non-human animals for producing human antibodies specific for human antigens
INVENTOR(S): **Lonberg, Nils**; Kay, Robert M.
PATENT ASSIGNEE(S): Genpharm International, USA
SOURCE: U.S., 314 pp., Cont.-in-part of U.S. Ser. No. 728,463.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6300129	B1	20011009	US 1996-758417	19961202
EP 814159	A2	19971229	EP 1997-201755	19910828
EP 814159	A3	19990714		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE

JP 11206387	A2	19990803	JP 1998-126859	19910828
US 5569825	A	19961029	US 1991-810279	19911217
US 5789650	A	19980804	US 1992-853408	19920318
US 5545806	A	19960813	US 1992-990860	19921216
US 5814318	A	19980929	US 1993-96762	19930722
JP 08140528	A2	19960604	JP 1994-289067	19941028
US 5625126	A	19970429	US 1994-352322	19941207
US 5770429	A	19980623	US 1995-544404	19951010
WO 9824884	A1	19980611	WO 1997-US21803	19971201

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9856881	A1	19980629	AU 1998-56881	19971201
EP 942959	A1	19990922	EP 1997-953058	19971201

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LV, FI, RO

JP 2001527386	T2	20011225	JP 1998-525687	19971201
US 6255458	B1	20010703	US 1998-42353	19980313

PRIORITY APPLN. INFO.:
US 1990-574748 B2 19900829
US 1990-575962 B2 19900831
US 1991-810279 A2 19911217
US 1992-853408 A2 19920318
US 1992-904068 B2 19920623
US 1992-990860 A2 19921216
US 1993-53131 A2 19930426
US 1993-96762 A2 19930722
US 1993-155301 B2 19931118
US 1993-161739 B2 19931203
US 1993-165699 B2 19931210
US 1994-209741 B2 19940309
US 1994-352322 A2 19941207
US 1995-544404 A2 19951010
US 1996-728463 A2 19961010
EP 1991-916470 A3 19910828
JP 1991-515142 A3 19910828
WO 1991-US6185 A 19910828
US 1992-834539 A2 19920205
WO 1992-US10983 A 19921217
WO 1994-US4580 A 19940425
US 1996-758417 A 19961202
WO 1997-US21803 W 19971201

AB The invention relates to transgenic non-human animals capable of producing heterologous antibodies and methods for producing human sequence antibodies which bind to human antigens with substantial affinity. Transgenes contg. all or portions of the human Ig heavy and light chain loci, or transgenes contg. synthetic "miniloci" which comprise essential functional elements of the human heavy and light chain loci, are employed to produce a transgenic nonhuman animal. Such a transgenic nonhuman animal has the capacity to produce Ig chains that are encoded by human Ig genes, and addnl. are capable of making an immune response against human antigens. Such transgenic animals can serve as a source of immune sera reactive with specified human antigens, and B-cells form such transgenic animals can be fused with myeloma cells to produce hybridomas that secrete monoclonal antibodies that are encoded by human Ig genes and which are

specifically reactive with human antigens. Thus, functional human light chain V segments are successfully introduced into the mouse genome by co-injection of a human .kappa. light chain minlocus and a YAC clone comprise multiple human V78 segments. The V78 segment genes contained on the YAC contribute to the expressed repertoire of human .kappa. chains in the resultant mouse. This example demonstrates a method for the repertoire expansion of transgene-encoded human Ig proteins, and specifically shows how a human .kappa. chain variable region repertoire can be expanded by co-introduction of unlinked polynucleotides comprising human Ig variable region segments.

REFERENCE COUNT: 123 THERE ARE 123 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:594996 CAPLUS
DOCUMENT NUMBER: 131:227650
TITLE: Recombination and class switch for human immunoglobulin transgenes in mouse
INVENTOR(S): **Lonberg, Nils**; Fishwild, Dianne M.; Ball, William J., Jr.
PATENT ASSIGNEE(S): Genpharm International, Inc., USA
SOURCE: PCT Int. Appl., 484 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9945962	A1	19990916	WO 1999-US5535	19990312
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 11206387	A2	19990803	JP 1998-126859	19910828
US 6255458	B1	20010703	US 1998-42353	19980313
AU 9930864	A1	19990927	AU 1999-30864	19990312

PRIORITY APPLN. INFO.:

US 1998-42353	A1	19980313
US 1990-574748	B2	19900829
US 1990-575962	B2	19900831
JP 1991-515142	A3	19910828
US 1991-810279	A2	19911217
US 1992-834539	A2	19920205
US 1992-853408	A2	19920318
US 1992-904068	B2	19920623
US 1992-990860	A2	19921216
US 1993-53131	A2	19930426
US 1993-96762	A2	19930722
US 1993-155301	B2	19931118
US 1993-161739	B2	19931203
US 1993-165699	B2	19931210
US 1994-209741	B2	19940309
US 1994-352322	A2	19941207
US 1995-544404	A2	19951010
US 1996-728463	A2	19961010
US 1996-758417	A2	19961202
WO 1999-US5535	W	19990312

AB The authors disclose the generation of transgenic non-human animals (i.e., mice) capable of producing heterologous human antibodies. The transgenic mice exhibit V(D)J recombination, class switching, and affinity maturation in response to immunization. Endogenous gene expression is prevented by homologous recombination or other ablative or suppressive methods. In one example, mice bearing human heavy chain transgenes and immunized with human carcinoembryonic antigen produced CEA-specific IgM. In a second example, mice bearing both heavy chain and light chain transgenes and immunized with human **CD4** produced a primary anti-**CD4** IgM response and, on subsequent reimmunization, a secondary anti-**CD4** IgG response.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:398397 CAPLUS
DOCUMENT NUMBER: 129:66838
TITLE: Transgenic non-human animals capable of producing heterologous antibodies
INVENTOR(S): **Lonberg, Nils**; Kay, Robert M.
PATENT ASSIGNEE(S): Genpharm International, USA
SOURCE: PCT Int. Appl., 453 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9824884	A1	19980611	WO 1997-US21803	19971201
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 11206387	A2	19990803	JP 1998-126859	19910828
US 6300129	B1	20011009	US 1996-758417	19961202
AU 9856881	A1	19980629	AU 1998-56881	19971201
EP 942959	A1	19990922	EP 1997-953058	19971201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LV, FI, RO				
JP 2001527386	T2	20011225	JP 1998-525687	19971201

PRIORITY APPLN. INFO.:

US 1996-758417	A	19961202
US 1990-574748	B2	19900829
US 1990-575962	B2	19900831

JP 1991-515142 A3 19910828
US 1991-810279 A2 19911217
US 1992-853408 A2 19920318
US 1992-904068 B2 19920623
US 1992-990860 A2 19921216
US 1993-53131 A2 19930426
US 1993-96762 A2 19930722
US 1993-155301 B2 19931118
US 1993-161739 B2 19931203
US 1993-165699 B2 19931210
US 1994-209741 B2 19940309
US 1994-352322 A2 19941207
US 1995-544404 A2 19951010
US 1996-728463 A2 19961010
WO 1997-US21803 W 19971201

AB The invention relates to transgenic non-human animals capable of producing heterologous antibodies and methods for producing human sequence antibodies which bind to human antigens with substantial affinity. The antigens described above are human carcinoembryonic antigen, human CD4, and human interleukin 8. The produced heterologous antibodies comprise a VH4-34 (or VH5-51) segment, a JH5 (or JH2) segment, a heavy chain CDR3 region comprising VINWFDP (or PANWNWYFVL), a VkL19 (or VkL18) segment, a Jk2 (or JK4) segment, and a light chain CD3 region comprising the sequence QQANSFPYT (or QQFISYPQLT).

L3 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:435738 CAPLUS
DOCUMENT NUMBER: 129:94468
TITLE: Transgenic non-human animals capable of producing heterologous antibodies
INVENTOR(S): **Lonberg, Nils**; Kay, Robert M.; et al.
PATENT ASSIGNEE(S): GenPharm International, Inc., USA
SOURCE: U.S., 173 pp. Cont.-in-part of U. S. 5,625,126.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5770429	A	19980623	US 1995-544404	19951010
WO 9203918	A1	19920319	WO 1991-US6185	19910828
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RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
EP 814159	A2	19971229	EP 1997-201755	19910828
EP 814159	A3	19990714		
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JP 11206387	A2	19990803	JP 1998-126859	19910828
US 5569825	A	19961029	US 1991-810279	19911217
US 5789650	A	19980804	US 1992-853408	19920318
US 5545806	A	19960813	US 1992-990860	19921216
WO 9312227	A1	19930624	WO 1992-US10983	19921217
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RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
US 5814318	A	19980929	US 1993-96762	19930722
WO 9425585	A1	19941110	WO 1994-US4580	19940425
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JP 08140528	A2	19960604	JP 1994-289067	19941028
US 5625126	A	19970429	US 1994-352322	19941207
CA 2232813	AA	19970417	CA 1996-2232813	19961010
WO 9713852	A1	19970417	WO 1996-US16433	19961010
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RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
AU 9711149	A1	19970430	AU 1997-11149	19961010
AU 729290	B2	20010201		
EP 854917	A1	19980729	EP 1996-941938	19961010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1199422	A	19981118	CN 1996-197554	19961010
JP 2000502324	T2	20000229	JP 1997-515285	19961010
US 6300129	B1	20011009	US 1996-758417	19961202
US 6255458	B1	20010703	US 1998-42353	19980313

PRIORITY APPLN. INFO.:
US 1990-574748 B2 19900829
US 1990-575962 B2 19900831
WO 1991-US6185 A 19910828
US 1991-810279 A2 19911217
US 1992-853408 A2 19920318
US 1992-904068 A2 19920623
US 1992-990860 A2 19921216
WO 1992-US10983 A 19921217
US 1993-53131 A2 19930426
US 1993-96762 B2 19930722
US 1993-155301 B2 19931118
US 1993-161739 B2 19931203
US 1993-165699 B2 19931210
US 1994-209741 B2 19940309
WO 1994-US4580 A 19940425
US 1994-352322 A2 19941207
EP 1991-916470 A3 19910828
JP 1991-515142 A3 19910828
US 1992-834539 A2 19920205
US 1995-544404 A 19951010
US 1996-728463 A2 19961010
WO 1996-US16433 W 19961010
US 1996-758417 A2 19961202

AB The invention relates to transgenic non-human animals capable of producing heterologous antibodies and methods for producing human sequence antibodies which bind to human antigens with substantial affinity. Thus, demonstrated were construction of vector pGPe, IgM/IgG-expressing minilocus transgene pHC2 encoding human VHI family gene VH49.8, redn. of

endogenous mouse Ig expression by antisense RNA, immunization and immune response (to dinitrophenyl and human carcinoembryonic antigen) in a transgenic mouse of present invention, targeted inactivation of murine .lambda. light chain locus and heavy chain locus, class switching and somatic mutation and B cell development in immunized transgenic mice homozygous for an inactivated endogenous Ig. locus and contg. HC1 or HC2 heavy chain transgenes, immunization with human CD4 and IgE, among others.

L3 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:361724 CAPLUS
DOCUMENT NUMBER: 126:326445
TITLE: Transgenic non-human animals capable of producing human or other heterologous antibodies specific for human antigens such as CD4
INVENTOR(S): **Lonberg, Nils**; Kay, Robert M.
PATENT ASSIGNEE(S): Genpharm International, Inc., USA; Lonberg, Nils; Kay, Robert M.
SOURCE: PCT Int. Appl., 394 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 15
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9713852	A1	19970417	WO 1996-US16433	19961010
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
JP 11206387	A2	19990803	JP 1998-126859	19910828
US 5770429	A	19980623	US 1995-544404	19951010
AU 9711149	A1	19970430	AU 1997-11149	19961010
AU 729290	B2	20010201		
EP 854917	A1	19980729	EP 1996-941938	19961010
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2000502324	T2	20000229	JP 1997-515285	19961010

PRIORITY APPLN. INFO.:

US 1995-544404	A2	19951010
US 1990-574748	B2	19900829
US 1990-575962	B2	19900831
JP 1991-515142	A3	19910828
WO 1991-US6185	A	19910828
US 1991-810279	A2	19911217
US 1992-853408	A2	19920318
US 1992-904068	A2	19920623
US 1992-990860	A2	19921216
WO 1992-US10983	A	19921217
US 1993-53131	A2	19930426
US 1993-96762	B2	19930722
US 1993-155301	B2	19931118
US 1993-161739	B2	19931203
US 1993-165699	B2	19931210
US 1994-209741	B2	19940309
WO 1994-US4580	A	19940425
US 1994-352322	A2	19941207
WO 1996-US16433	W	19961010

AB The invention relates to transgenic non-human animals capable of producing heterologous antibodies and methods for producing human sequence antibodies which bind to human antigens with substantial affinity. Several plasmid vectors are described and Ig-specifying DNA sequences are included. Esp., human CD4 antigen-specific antibodies are emphasized.

L3 ANSWER 7 OF 11 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 1998294464 MEDLINE
DOCUMENT NUMBER: 98294464 PubMed ID: 9631008
TITLE: High-avidity human IgG kappa monoclonal antibodies from a novel strain of minilocus transgenic mice.
COMMENT: Comment in: Nat Biotechnol. 1996 Jul;14(7):826
AUTHOR: Fishwild D M; O'Donnell S L; Bengoechea T; Hudson D V; Harding F; Bernhard S L; Jones D; Kay R M; Higgins K M; Schramm S R; **Lonberg N**
CORPORATE SOURCE: Department of Hybridoma Development, GenPharm International, Mountain View, CA 94043, USA.. dfishwild@genpharm.com
SOURCE: NATURE BIOTECHNOLOGY, (1996 Jul) 14 (7) 845-51.
Journal code: CQ3; 9604648. ISSN: 1087-0156.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199807
ENTRY DATE: Entered STN: 19980716
Last Updated on STN: 19980716
Entered Medline: 19980707

AB Human immunoglobulin transgenic mice provide a method of obtaining human monoclonal antibodies (Mabs) using conventional hybridoma technology. We describe a novel strain of human immunoglobulin transgenic mice and the use of this strain to generate multiple high-avidity human sequence IgG kappa Mabs directed against a human antigen. The light chain transgene is derived in part from a yeast artificial chromosome clone that includes nearly half of the germline human V kappa region. In addition, the heavy-chain transgene encodes both human mu and human gamma 1 constant regions, the latter of which is expressed via intratransgene class switching. We have used these animals to isolate human IgG kappa Mabs that are specific for the human T-cell marker CD4, have high binding avidities, and are immunosuppressive in vitro. The human Mab-secreting hybridomas display properties similar to those of wild-type mice including stability, growth, and secretion levels. Mabs with four distinct specificities were derived from a single transgenic mouse, consistent with an extensive diversity in the primary repertoire encoded by the transgenes.

L3 ANSWER 8 OF 11 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1996:502150 BIOSIS
DOCUMENT NUMBER: PREV199699224506
TITLE: High avidity human IgG-kappa anti-CD4 monoclonal

antibodies from a novel strain of minilocus transgenic mice.

AUTHOR(S): Fishwild, Dianne M.; O'Donnell, Susan L.; Bengoechea, Tasha; Hudson, Debra V.; Harding, Fiona; Bernhard, Susan L.; Jones, Debbie; Kay, Robert M.; Higgins, Kay M.; Schramm, Stephen R.; **Lonberg, Nils**

CORPORATE SOURCE: GenPharm Int., Mountain View, CA 94043 USA

SOURCE: Arthritis & Rheumatism, (1996) Vol. 39, No. 9 SUPPL., pp. S285.
Meeting Info.: 60th National Scientific Meeting of the American College of Rheumatology and the 31st National Scientific Meeting of the Association of Rheumatology Health Professionals Orlando, Florida, USA October 18-22, 1996
ISSN: 0004-3591.

DOCUMENT TYPE: Conference

LANGUAGE: English

L3 ANSWER 9 OF 11 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.DUPLICATE 2

ACCESSION NUMBER: 95109876 EMBASE

DOCUMENT NUMBER: 1995109876

TITLE: Over-expression of CD3.epsilon. transgenes blocks T lymphocyte development.

AUTHOR: Wang B.; Levelt C.; Salio M.; Zheng D.; Sancho J.; Liu C.-P.; She J.; Huang M.; Higgins K.; Sunshine M.-J.; Eichmann K.; Lacy E.; **Lonberg N.**; Terhorst C.

CORPORATE SOURCE: Division of Immunology, Beth Israel Hospital, Harvard Medical School,Boston, MA 02115, United States

SOURCE: International Immunology, (1995) 7/3 (435-448).
ISSN: 0953-8178 CODEN: INIMEN

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 021 Developmental Biology and Teratology
022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB We have reported previously that mice carrying >30 copies of the human CD3.epsilon. transgene completely lose their T lymphocytes and NK cells (36). Here we demonstrate by immunohistology that in the most severely immunodeficient mouse, tg.epsilon.26, the thymus is very small, has sizeable vacuoles and does not contain recognizable T lymphocytes except for a small percentage of Thy-1+ cells and B cells. Cell surface phenotyping and TCR.alpha. and -.beta. rearrangement studies confirm that the arrest in T lymphocyte development precedes the arrest in rag-1(null), rag-2(null) and TCR.beta.(null) mice. Since the T cell progenitors in which the arrest occurred were absent in the transgenic mice, indirect approaches were taken to examine the causes of the block in T cell development. Analyses of 12 independently established mutant mouse lines, generated with five different transgenic constructs, revealed that the severity of the abrogation in T cell development was dependent on the number of copies of transgenes. Since the number of transgene copies generally correlated with the levels of expression of the transgenic CD3.epsilon. proteins, we concluded that over-expression of the CD3.epsilon. protein was the likely cause of the block in T lymphocyte development. The T cell immunodeficiency was caused by either the human or the murine CD3.epsilon. protein. Since transgene coded mRNAs were found in significantly higher quantities than endogenous CD3.epsilon. mRNAs in fetal thymi on days 13 and 14 of gestation, over-expression took place very early in development, probably prematurely. Over-expression of the CD3.epsilon. transgene in thymocyte precursors may therefore affect T lymphocyte development in the absence of TCR and possibly in the absence of the other CD3 proteins. More importantly, over-expression of the CD3.epsilon. protein in thymocytes of mice with a low copy number of transgenes had a significant effect on late thymic development. Over-expression of the CD3.epsilon. protein in immature thymocytes mimicked the effects caused by exposure of CD4-CD8-thymocytes to anti-CD3.epsilon. treatment: apoptosis and lack of TCR.beta. expression. We therefore speculate that in the homozygous tg.epsilon.26 animals the arrest in T cell development was caused by excessive signal transduction events rather than by a toxic effect of the transgenic protein.

L3 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:689851 CAPLUS

DOCUMENT NUMBER: 123:81582

TITLE: Transgenic non-human animals expressing human immunoglobulin genes and capable of producing human antibodies by isotype switching

INVENTOR(S): **Lonberg, Nils**; Kay, Robert M.

PATENT ASSIGNEE(S): Genpharm International, Inc., USA

SOURCE: PCT Int. Appl., 295 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 15

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9425585	A1	19941110	WO 1994-US4580	19940425
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KR, KZ, LK, LU, LV, MG, MN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, CF, CG, CI, CM, GA, GN, ML				
JP 11206387	A2	19990803	JP 1998-126859	19910828
US 5814318	A	19980929	US 1993-96762	19930722
AU 9468194	A1	19941121	AU 1994-68194	19940425
JP 08509612	T2	19961015	JP 1994-524481	19940425
EP 754225	A1	19970122	EP 1994-916581	19940425
R: AT, BE, CH, DE, DK, ES, FR, GB, LI				
JP 08140528	A2	19960604	JP 1994-289067	19941028
US 5770429	A	19980623	US 1995-544404	19951010

PRIORITY APPLN. INFO.:

US 1993-53131	A	19930426
US 1993-96762	A	19930722
US 1993-155301	A	19931118
US 1993-161739	A	19931203
US 1993-165699	A	19931210
US 1994-209741	A	19940309
US 1990-574748	B2	19900829
US 1990-575962	B2	19900831
JP 1991-515142	A3	19910828
WO 1991-US6185	A	19910828

US 1991-810279 A2 19911217
US 1992-853408 A2 19920318
US 1992-904068 A2 19920623
US 1992-990860 A2 19921216
WO 1992-US10983 A 19921217
US 1993-156739 A 19931203
WO 1994-US4580 A 19940425
US 1994-352322 A2 19941207

AB Transgenic non-human animals capable of producing heterologous antibodies are prepd. and their use in the prepn. of antibodies that bind to human antigens with substantial affinity are described. These animals generate B cell precursors that present IgM on their surfaces and so are capable of maturing and are capable of isotype switching. Animals producing a single human antibody and not capable of isotype switching may also be prepd. The ability to recombine is ensured by taking care to ensure that sequences involved in the recombination process are introduced as part of the transforming DNA. The expression of endogenous Ig genes may be suppressed either by disruption of essential loci, by antisense methods, or using antibodies to endogenous Igs. Chimeric antibodies, e.g. with host organism const. regions, may also be prepd. if the endogenous genes are not inactivated. The construction of such genes and the prepn. of transgenic mice that synthesize and secrete human Igs is demonstrated. The prepn. of hybridomas secreting human monoclonal antibodies to **CD4** antigen is also demonstrated.

L3 ANSWER 11 OF 11 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 88261303 MEDLINE
DOCUMENT NUMBER: 88261303 PubMed ID: 3260331
TITLE: Mouse brain **CD4** transcripts encode only the COOH-terminal half of the protein.
AUTHOR: **Lonberg N**; Gettner S N; Lacy E; Littman D R
CORPORATE SOURCE: DeWitt Wallace Research Laboratory, Memorial Sloan-Kettering Cancer Center, New York, New York 10021.
CONTRACT NUMBER: AI 23513 (NIAID)
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (1988 May) 8 (5) 2224-8. Journal code: NGY; 8109087. ISSN: 0270-7306.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-M20265
ENTRY MONTH: 198807
ENTRY DATE: Entered STN: 19900308
Last Updated on STN: 19970203
Entered Medline: 19880729

AB The T-cell surface glycoprotein **CD4** is thought to function as a receptor for class II major histocompatibility complex molecules. Human **CD4** is also the lymphoid cell receptor for human immunodeficiency virus, the causative agent of acquired immune deficiency syndrome. The observed infection of the central nervous system in acquired immune deficiency syndrome patients raises the possibility that **CD4** is also present in nerve tissue and that a cell surface receptor for class II major histocompatibility complex antigens could play a role in central nervous system function. This possibility is reinforced by the detection of unique **CD4**-related transcripts in mouse and human brain tissue. In this study, the structure of the mouse brain **CD4** transcript was determined. It is identical to the last two-thirds of the **CD4** message and is capable of encoding a 217-residue protein that would consist of a truncated, 154-residue, cell surface region, together with the complete **CD4** transmembrane and cytoplasmic regions. It would not include an amino-terminal hydrophobic leader peptide.

```
=> s  antibod? near CD4
L4            0 ANTIBOD? NEAR CD4

=> s  antibod? (P) CD4
L5        41385 ANTIBOD? (P) CD4

=> s l5 and (10C5 or 4D1)
L6            0 L5 AND (10C5 OR 4D1)

=> dis his

     (FILE 'HOME' ENTERED AT 09:11:15 ON 14 MAR 2002)

     FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 09:11:41 ON 14 MAR 2002
L1          160 S LONBERG N?/AU OR KAY/AU
L2           16 S L1 AND CD4
L3           11 DUP REM L2 (5 DUPLICATES REMOVED)
L4            0 S  ANTIBOD? NEAR CD4
L5        41385 S  ANTIBOD? (P) CD4
L6            0 S L5 AND (10C5 OR 4D1)

=> end
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
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COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
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FULL ESTIMATED COST                                     42.22      42.37

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                                                        ENTRY    SESSION
CA SUBSCRIBER PRICE                                     -4.34      -4.34

STN INTERNATIONAL LOGOFF AT 09:18:34 ON 14 MAR 2002
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dis his

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FILE 'MEDLINE, CAPLUS, EMBASE, BIOSIS' ENTERED AT 09:11:41 ON 14 MAR 2002

L1	160	S	LONBERG N?/AU OR KAY/AU
L2	16	S	L1 AND CD4
L3	11		DUP REM L2 (5 DUPLICATES REMOVED)
L4	0	S	ANTIBOD? NEAR CD4
L5	41385	S	ANTIBOD? (P) CD4
L6	0	S	L5 AND (10C5 OR 4D1)